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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/747,865	12/29/2003	Benjamin Oshlack	200.1134 CON	2763

7590 11/15/2005
Davidson, Davidson & Kappel, LLC
14th Floor
485 Seventh Avenue
New York, NY 10018

EXAMINER

RUSSEL, JEFFREY E

ART UNIT PAPER NUMBER

1654

DATE MAILED: 11/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/747,865	Applicant(s) OSHLACK ET AL.	
	Examiner Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,9-12,20 and 40-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,9-12,20 and 40-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>20050728</u> . | 6) <input type="checkbox"/> Other: _____ |

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1. Instant claims 1, 9-12, 20, and 40-45 are deemed not to be entitled under 35 U.S.C.

119(e) to the benefit of the filing date of provisional application 60/181,358 because the provisional application, under the test of 35 U.S.C. 112, first paragraph, does not disclose the release of sub-analgesic amounts of the opioid agonist; and does not disclose opioid antagonists in amounts as low as 1000 fold less than the amounts of opioid agonist. Accordingly, the WO Patent Application 99/32120 and the WO Patent Application 00/01377 are available as prior art against these claims under 35 U.S.C. 102(b).

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 1, 9-12, 20, and 40-45 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 99/32120 in view of Crain et al (U.S. Patent No. 5,767,125) and further in view of the WO Patent Application 00/01377 or Simon (U.S. Patent No. 6,103,258). The WO Patent Application '120 teaches oral dosage forms of an opioid analgesic, which can be in sustained release form and which comprise a combination of an opioid agonist and an opioid antagonist. In particular, the opioid agonist can be hydromorphone, oxycodone, morphine, or hydrocodone, and the opioid antagonist can be naltrexone or naloxone. See, e.g., the Abstract; page 8, lines 1-9; page 11, lines 17-31; and page 13, lines 10-13 and 28-31. Use of the combination of opioid agonist and antagonist reduces the abuse potential of the opioid agonist and attenuates the possibility of physical dependence upon the opioid agonist (see, e.g., page 6, lines 5-12, and page 8, lines 14-24). The sustained release form permits administration on a twice-a-day or a once-a-day basis and can provide analgesia for about 24 hours (see, e.g., page 8, lines 25-28, and page 21, lines 21-25). The sustained release carrier can be present either a

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matrix or as a coating, and the oral dosage form can be granules, spheroids, beads, or pellets (see, e.g., page 8, line 25 - page 9, line 1, and page 20, lines 10-11). The WO Patent Application '120 teaches the oral administration of combinations of opioid agonists and opioid antagonists where the opioid antagonist reduces the abuse potential of and attenuates physical dependence upon the opioid agonist, but does not teach amounts of opioid antagonists which enhance the potency of the opioid agonist or which reduce side effects of the opioid agonist such as anti-analgesia, hyperalgesia, hyperexcitability, and tolerance, and does not teach opioid antagonist amounts of 100 to about 1000 fold less than the amounts of opioid agonist. Crain et al teach the oral administration of combinations of opioid agonists and opioid antagonists where the opioid antagonist enhances the potency of the opioid agonist and reduces the side effects of the opioid agonist such as anti-analgesia, hyperalgesia, hyperexcitability, and tolerance. To achieve these results, Crain et al administer their opioid antagonists in amounts at least 100-1000 fold less than the amount of the opioid agonist. Because of the potency-enhancing effect of the opioid antagonist, lesser amounts, including sub-analgesic amounts, of the opioid agonist can be used. See, e.g., the Abstract; column 5, lines 9-22 and 41-47; column 6, lines 7-36; and claim 4. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the opioid agonists and antagonists of the WO Patent Application '120 in the amounts and proportions taught Crain et al because Crain et al's amounts and proportions are taught to be applicable to a wide variety of administration means, and because Crain et al's proportions provide the benefit of enhanced potency of the opioid agonist while permitting the use of lower amounts and with fewer side effects while still achieving a goal of the WO Patent Application '120 of reducing the specific side effect of physical dependence on the opioid

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agonist. The WO Patent Application '120 does not teach releasing the opioid agonist and antagonist at substantially proportionate rates. The WO Patent Application '377 teaches co-administration of opioid agonists and antagonists by intramuscular, intravenous, nasal, oral, sublingual or transdermal methods, recognizes that the individual components can have different pharmacokinetic profiles and different in vivo life spans, and teaches providing a controlled release matrix or coating to the shorter-acting component so that its pharmacokinetic profile better matches the profile of the longer-acting component, i.e. so that their release rates are proportional. See, e.g., page 17, line 22 - page 18, line 26; page 22, lines 20-22; page 22, line 30 - page 23, line 8. Simon is the U.S. equivalent of the WO Patent Application 00/01377 and contains the same disclosure as that of the WO Patent Application '377 (see, e.g., column 9, line 39 - column 10, line 18, and column 12, lines 33-60). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to provide controlled release matrices or coatings as taught by the WO Patent Application '377 and Simon to the agonist or antagonist of the WO Patent Application '120 so that the problem of different pharmacokinetic profiles and in vivo lifespans is avoided.

4. Applicant's arguments filed July 28, 2005 have been fully considered but they are not persuasive.

The combination of references applied in the rejection set forth above is the same combination of references applied in section 13 of the Office action mailed January 27, 2005. Applicants did not provide any arguments traversing the rejection set forth in the previous Office action, and accordingly the rejection is maintained.

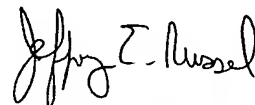
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5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Bruce Campell can be reached at (571) 272-0974. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.



Jeffrey E. Russel
Primary Patent Examiner
Art Unit 1654

JRussel
November 10, 2005